July 13, 2018

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NCI Technology Transfer Center
Email: *rose.freel@nih.gov.*

Re: Prospective Grant of an Exclusive Patent License: Development of an Anti-Mesothelin Chimeric Antigen Receptor (CAR) for the Treatment of Human Cancer to Atara Biotherapeutics Inc.

Dear Dr. Rose M. Freel:

We are writing to provide comments on the prospective grant of an exclusive patent license for the development of an anti-mesothelin Chimeric Antigen Receptor (CAR) for the treatment of human cancer to Atara Biotherapeutics Inc., as noticed in the Federal Register: 83 FR 30448.

According to the notice in the *Federal Register,* "the prospective exclusive license territory may be worldwide," and the field of use is described as:

> "The development of a mesothelin chimeric antigen receptor (CAR)-based immunotherapy using autologous or allogeneic T cells either transduced with a retroviral vector (including lentiviral vectors) or modified using a gene-editing technology, wherein the vector expresses a CAR comprising:
>
> (1) Single antigen specificity for binding to mesothelin, and
>
> (2) at least (a) the complementary determining region (CDR) sequences of the anti-mesothelin antibody known as m912, and (b) a T cell signaling domain; for the prophylaxis and treatment of mesothelin-expressing human cancers.'"

The NIH has been asked but declined to extend the comment period so that the public would have had additional time to obtain information from the NIH or third parties on the budgets of clinical trials for either CAR T-cell trials, or trials involving anti-mesothelin therapies, or both. Related to this, the NIH has been asked for information regarding the budgets of 14 CAR T trials funded by the NIH, and that information is unfortunately not yet available.

Information about the costs of conducting CAR T trials is important in evaluating the proposal by the NIH to grant an exclusive license and the scope of rights included in any exclusive license (as is required by 35 USC § 209), including the years of exclusivity and the safeguards to ensure that the patented products, services or procedures are available to the public on reasonable terms (as is required by 35 USC § 201(f)). We suggest the NIH take measures to increase the transparency of the costs of R&D that the NIH funds. Our comments for this license

contain suggestions that would increase transparency going forward, not only for R&D funded directly by the NIH, but also for R&D associated with the development of patented inventions owned by the NIH and licensed to third parties.

In the absence of public evidence that the NIH has estimated the costs of bringing this technology to market and evaluated the scope of rights necessary to induce such investment, we cannot support an exclusive license at this time.

If the NIH does in fact proceed with an exclusive license, these are provisions that we recommend be included in the terms of the license.

1. No discrimination against US residents in pricing

Prices in the U.S. for any drug, vaccine, medical device or other health technology using the invention should not be higher than the median price charged in the seven countries with the largest gross domestic product (GDP), that also have a per capita income of at least 50 percent of the United States, as measured by the World Bank Atlas Method.

2. Reduce term of exclusivity when revenues are large

The exclusivity of the license in the U.S. should be reduced by one year for every $500 million in revenue equivalents, earned after the first $1 billion, where revenue equivalent is defined as global cumulative sales plus market entry rewards as well as government grants or tax credits, for the product or products using the invention. The NIH could consider different benchmarks, based upon evaluating evidence of the costs of additional development of CAR T therapies, but the $1 billion and $.5 billion figures are at least a start to acknowledge that at some point, the returns on a government-funded invention are excessive, given the licensee's risk-adjusted investments.

3. Developing countries

The license should not be exclusive for countries with a per capita income that is less than 30 percent of the U.S.A. If the NIH does in fact provide exclusive rights in developing countries, the license holder should have an obligation to provide the NIH with a reasonable plan to make the drugs affordable and accessible in those countries, a condition the Gates Foundation has used for some patent licenses. In addition, if the licenses are exclusive in developing countries, the NIH should retain an explicit option to provide an additional license to the Medicines Patent Pool, if access is deemed insufficient in countries with incomes significantly lower than the United States.

5. Transparency

The licensee should be required to file an annual report to the NIH, available to the public, on the research and development (R&D) costs associated with the development of any product that uses the invention, including reporting separately the outlays on each clinical trial. We will note that this is not a request to see a company business plan or license application. We are asking that going forward the company be required to report on actual R&D outlays to develop the subject inventions. We recognize that 35 USC § 209(f) requires applicants to provide a

development plan and that such a plan is not subject to FOIA, and that the regulations regarding reports relating to the development plan are also limited as to the scope of and access to the reports, under 37 CFR 404.14 - Confidentiality of information, and that reports required under 37 CFR 404.5(b)(6) are considered confidential information. However, the NIH can ask for other reports, which can be made public. For example, the NIH required reports from the Icahn School of Medicine at Mount Sinai on access to Fabrazyme, and those reports were eventually made public under FOIA. The federal government needs to revise the regulations regarding the confidentiality of reporting of federally funded inventions, but even now, as the Fabrazyme case illustrates, there may be some flexibility, particularly in this case, where the reports are not specifically related to the company's development plan, and such transparency is clearly in the public interest.

Sincerely,

Health Action International (HAI)
Health GAP
Interfaith Center on Corporate Responsibility (ICCR)
Knowledge Ecology International (KEI)
People of Faith for Access to Medicines (PFAM)
Social Security Works (SSW)
Union for Affordable Cancer Treatment (UACT)
Universities Allied for Essential Medicines (UAEM)